UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/824,053	04/03/2001	Peter Stougaard	PF347D1	9289

7590 09/09/2003

Hunton & Williams
Intellectual Property Department
1900 K Street, NW
Suite 1200
Washington, DC 20006-1109

EXAMINER
MOORE, WILLIAM W

ART UNIT	PAPER NUMBER
1652	13

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/824,053	STOUGAARD ET AL.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-25,32-41 and 43-84* is/are pending in the application.

4a) Of the above claim(s) *36-41,43,44 and 70-82* is/are withdrawn from consideration.

5)☒ Claim(s) *84* is/are allowed.

6)☒ Claim(s) *9-25, 32-35, 45-69, and 83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Amendment

Applicant's Amendment B, Paper No. 12 filed June 16, 2003, has been entered, adding new claims 83 and 84 and amending claims 9, 45 and 50. While Paper No. 12 indicates, at page 1, that claim 32 is to be amended, no amendment of this claim is presented. For reasons set forth below, amendments to claims 45 and 50 do not overcome the rejections of record of claims 45-69 under 35 U.S.C. §§101 and 112, first and second paragraphs, for lack of utility, lack of enablement as to use, and for lack of a definite description, of a "substance" stated in the communication mailed January 16, 2003. These rejections of record are also extended to the new claim 83. Applicant's Terminal Disclaimer filed June 16, 2003, renders the double-patenting rejection of record moot. Claims 26-31, 36-41, 43, 44, and 69-82 remain withdrawn from consideration as drawn to a non-elected invention and claims 9-25, 32-35, 45-69, 83 and 84 are examined to the extent they describe a polypeptide having, and compositions comprising a polypeptide having, hexose oxidase activity, wherein the polypeptide comprises at least the peptide of SEQ ID NO:3.

Information Disclosure Statement

The references not submitted with the Information Disclosure Statement [IDS] filed November 4, 2002, did not accompany the Amendment filed June 16, 2003. The IDS filed November 4, 2002, did not provide many documents cited therein thus did not comply with 37 CFR 1.98(a)(2). The IDS filed November 4, 2002, will be considered upon submission of the documents numbered 1-5, 11-14, 17, 19-32, 36, 37, and 44-94 on Applicant's PTO-Form 1449.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 45-69 and 83 are rejected, essentially for reasons of record, under 35 U.S.C. §101 because the claimed invention lacks patentable utility.

Applicant's arguments filed June 16, 2003, have been fully considered but they are not persuasive. Applicant suggests at page 5 of Paper No. 12 that the amended claim 45 has a recitation "consistent with the suggestion of the Examiner" in the communication mailed January 16, 2003. The amended claim 45 requires that a "substance" comprise a polypeptide having hexose oxidase activity, and the new claim 83 requires that a "substance" comprise the polypeptide with the amino acid sequence of SEQ ID NO:31. Neither claim provides recitations consistent with the suggestion made in the communication mailed January 16, 2003, again restated at the close of this rejection. A claimed invention must posses a specific, substantial, and credible *in vitro* or *in vivo* utility. In the communication mailed January 16, 2003, it was agreed that isolated polypeptides of claims 9-25 and 32-35 having hexose oxidase were not subject to this rejection because at least one such isolated polypeptides having hexose oxidase activity is disclosed and has utility. A composition of matter comprising such a polypeptide will also have utility. The specification discloses no "substances", whether polypeptides having hexose oxidase activity or compositions comprising substances wherein a polypeptide has hexose oxidase activity, and claims 45-69 and 83 do not require that a **composition** comprise a polypeptide of claims 9-25 and 32-35 that has hexose oxidase activity.

Instead, the specification discloses only "substances" that **expressly lack any polypeptide having hexose oxidase activity**. See, e.g., page 4, lines 5-7, ("or any other undesirable contaminating substances including undesirable algal pigments and environmental pollutants"), page 8, lines 27-28, ("adding substances such as e.g. $(NH_4)_2SO_4$ which causes the protein to precipitate"), page 20, lines 19-21, ("undesired contaminating substances originating from the cultivation medium, production host organisms or substances produced by these cells during cultivation"), page 22, lines 11-12, ("the range of carbohydrate substances which can be utilized as substrates") and at

lines 16-17, ("other carbohydrate substances including disaccharides"), the phrase that spans pages 25-26 ("substrate[s] . . . generated [include] . . . di-, oligo- or polysaccharides to lower sugar substances"), page 27, lines 30-32, ("silage additive such as lactic acid bacterial inoculants or enzymes which generate low molecular sugar substances"), page 33, lines, 18-19, ("reacts with the chromogenic substance, *o*-dianisidine to form a dye"), page 41, lines 3-4, ("red protein phycoerythrin and other coloured substances"), page 43, lines 30-31, ("to allow the thioglycolate to scavenge any amino-reactive substances", and page 51, lines 16-18, ("the 29 kD digest contained only small amounts of the contaminating substances eluting later than t = 83 min[utes]"). None of these contaminating, substrate, or reagent "substances" are polypeptides having hexose oxidase activity and none comprise polypeptides that have hexose oxidase activity. A method of using disclosed contaminating, substrate, or reagent "substances" for further research to determine, e.g., which substances, if any, might be able to incorporate in their chemical structure a polypeptide having hexose oxidase activity, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). Where the only disclosed "substances" upon which claims might be based are contaminants, substrates, or reagents, none of which comprise polypeptides having hexose oxidase activity, the specification establishes no specific utility for an undesignated substance that has somehow come to comprise a polypeptide having the ability to recognize and oxidize hexose sugars.

It is again noted that the specification discloses **compositions** that comprise the disclosed hexose oxidase having the amino acid sequence set forth in SEQ ID NO:31, which has hexose oxidase activity, and amending claims 45-69 to describe such **compositions** will avoid this rejection. The rejection of record is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45-69 and 83 are also rejected, essentially for reasons of record, under 35 U.S.C. §112, first paragraph. Applicant's arguments filed June 16, 2003, have been fully considered above but they are not persuasive. Specifically, since the claimed invention, which according to the specification is essentially either an undefined substance that is a contaminant, or a defined compound such as a saccharide or a dye precursor, cannot have hexose oxidase, the claimed subject matter is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The rejection of record is maintained.

Claims 9-25, 32-35, 45-69 and 83 are rejected for reasons of record under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed June 16, 2003, have been fully considered above but they are not persuasive. Applicant suggests at pages 5-6 of Paper No. 12 that the hexadecapeptide of SEQ ID NO:3 conveys sufficient structural and functional characteristics to establish Applicant's possession of a genus of molecules that must be at least ten-fold more massive, and much more complex, than the peptide of SEQ ID NO:3 in order to have the ability to recognize and act on, at least, hexose sugars. But the specification discloses that the peptide of SEQ ID NO:3 is part of a much larger molecule which inherently requires extensive secondary and tertiary structural features – features that a peptide the size of that set forth in SEQ ID NO:3 cannot possibly embody – in order to bind a hexose sugar and catalyze its oxidation. Thus, the specification cannot be considered to exemplify or describe the preparation of generic polypeptides that need

comprise no more specific structure than the hexadecapeptide of SEQ ID NO:3, and methods of use thereof, of claims 9-25 and 32-35, in order to function as hexose oxidases. It also does not exemplify or describe the preparation of subject matters of claims 45-69 that are generic substances – which according to the specification are either undefined contaminants, defined saccharide substrates, or a dye precursor – that may somehow comprise a hexadecapeptide of SEQ ID NO:3 and thereby exhibit hexose oxidase activity, and methods of use thereof, neither does it exemplify describe the subject matter of claim 83, a generic substance - which according to the specification is either an undefined contaminants, a defined saccharide substrates, or a dye precursor that comprises a polypeptide that has the amino acid sequence of SEQ ID NO:31. Instead, the specification describes but a single product that meets the functional limitation "having hexose oxidase activity", the hexose oxidase having the amino acid sequence set forth in SEQ ID NO:31, and compositions that comprise this product.

Claims 9-25, 32-35, and 45-69 reach generic polypeptides, or substances, comprising a peptide, which, itself, cannot be expected to support the functional limitation and claim 83 reaches some generic, undisclosed, substance that comprises a disclosed polypeptide having the amino acid sequence of SEQ ID NO:31 that has the required activity. The specification describes no design of such generic proteins, or generic substances, that are based on the peptide of SEQ ID NO:3, and does not suggest any location within such generic proteins for the peptide of SEQ ID NO:3, and the specification describes no design of a generic "substance" that comprises the polypeptide having the amino acid sequence of SEQ ID NO:31. The pertinent appellate decisions in the area of biotechnology were stated in the communication mailed January 16, 2003. Concerning the issue of whether a disclosure of how to obtain a polypeptide encoded by a nucleic acid sequence might describe undisclosed polynucleotides and their encoded products, the Court of Appeals for the Federal Circuit held that, "While one does not

need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). Concerning the issue of whether a description of a single species of disclosed polynucleotide and a single species of encoded polypeptide might constitute a description of other, undisclosed and divergent, polynucleotides and their undisclosed and divergent encoded polypeptides, the Court of Appeals for the Federal Circuit held that a claimed invention must be described with such "relevant identifying characteristic[s]" that the public could know that the inventor possessed the invention at the time an application for patent was filed, rather than by a mere "result that one might achieve if one had made that invention". *University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The specification's treatment of the claimed subject matter is considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could not predict the structure, or other properties, of the claimed products and claimed methods of use thereof, thus the rejection of record is sustained.

Claims 9-25, 32-35, 45-69 and 83, are for reasons of record rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a polypeptide having hexose oxidase activity and comprising the amino acid sequence set forth in SEQ ID NO:31, and for compositions comprising this polypeptide,

does not reasonably provide enablement for the preparation of a generic polypeptide, or a generic substance, that comprises no more definite structure than a peptide having the sequence of sixteen amino acids of SEQ ID NO:3, or the preparation of a generic substance that comprises the amino acid sequence set forth in SEQ ID NO:31. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments filed June 16, 2003, have been fully considered above but they are not persuasive. Applicant suggests at pages 5-6 of Paper No. 12 that the disclosure of the peptide of SEQ ID NO:3 in the specification together with its "disclosure[s] regarding specific primers, oligonucleotides, etc., and general and specific

procedures for preparing the claimed polypeptides" enable, at least, the recovery of others that may comprise the peptide of SEQ ID NO:3. Yet claims 9-25, 32-35, 45-69 and 83 contemplate not only further, native, *Chondrus crispus* hexose oxidases: they also contemplate the *de novo* design of a very broad genus of polypeptides wherein arbitrary amino acid substitutions, additions or deletions anywhere in an oxidase of any source are prepared so long as the resulting polypeptide, or some substance, comprises somewhere a sequence of sixteen amino acids represented by SEQ ID NO:3. Claim 83 contemplates redesigning undefined contaminants, defined saccharide substrates, or a dye precursor to incorporate the polypeptide of SEQ ID NO:31. There is no guidance or support in specification for the *de novo* design and preparation of generic polypeptides that have hexose oxidase activity and somewhere contain the specific hexadecapeptide having the amino acid sequence set forth in SEQ ID NO:3. Neither is there any guidance or support in the specification for the redesign of undefined contaminants, defined saccharide substrates, or a dye precursor so that there chemical structures might incorporate the amino acid sequence set forth in SEQ ID NO:31.

It is well settled that 35 U.S.C. §112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (recognizing and applying the "*Forman*" factors). Cf., *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) (citing eight factors relevant to analysis of enablement). The standard set by the CCPA, the precursor of the Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a reasonable correlation must exist between the scope asserted in the claimed subject matter and the scope of guidance the specification provides. *In re Fisher*, 427 F.2d 833, 839,

166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone); see also, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (functional equivalency of divergent gene products not supported by disclosure only of a single B-cell growth factor allele). The Federal Circuit approved the standard set by the CCPA in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997). The rejection of record is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 45-69 and 83 are rejected, essentially for reasons of record, under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is still unclear what is intended by the recitation of the amended claim 45, "[a] substance comprising . . . a polypeptide having hexose oxidase activity", particularly where "substances" disclosed in the specification **expressly lack any polypeptide having hexose oxidase activity**. See, e.g., page 4, lines 5-7, ("or any other undesirable contaminating substances including undesirable algal pigments and environmental pollutants"), page 8, lines 27-28, ("adding substances such as e.g. $(NH_4)_2SO_4$ which causes the protein to precipitate"), page 20, lines 19-21, ("undesired contaminating substances originating from the cultivation medium, production host organisms or substances produced by these cells during cultivation"), page 22, lines 11-12, ("the range of carbohydrate substances which can be utilized as substrates") and at lines 16-17, ("other carbohydrate substances including disaccharides"), the phrase that spans pages 25-26 ("substrate[s] . . . generated [include] . . . di-, oligo- or polysaccharides to lower sugar substances"), page 27, lines 30-32, ("silage additive such as lactic acid bacterial inoculants or enzymes which generate low molecular sugar substances"), page 33, lines, 18-19, ("reacts with the chromogenic substance, *o*-dianisidine to form a dye"), page 41, lines 3-4, ("red protein phycoerythrin

and other coloured substances"), page 43, lines 30-31, ("to allow the thioglycolate to scavenge any amino-reactive substances", and page 51, lines 16-18, ("the 29 kD digest contained only small amounts of the contaminating substances eluting later than t = 83 min[utes]"). None of these contaminating, substrate, or reagent "substances" are polypeptides having hexose oxidase activity and none comprise polypeptides that have hexose oxidase activity. Claims 46-69 are included in this rejection because they depend from claim 45 but do not otherwise resolve the ambiguities of claim 45. Claim 83 is included in this rejection because there are no contaminant, substrate, or reagent "substances" indicated to have a polypeptide with the amino acid sequence set forth in SEQ ID NO:31 disclosed or suggested in the specification.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached between 7:00AM-5:30PM EST on Mondays and Wednesdays, between 7:00AM-1:30PM EST on Tuesdays and Thursdays, and between 8:30AM and 5:00PM EST on Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached at 703.308.3804. Further fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
September 5, 2003

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600